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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,750	07/25/2005	Gregory B Martin	3213/104	6908

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,750	MARTIN ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *103-108,110 and 111* is/are pending in the application.

4a) Of the above claim(s) *105 and 106* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *103,104,107,108,110 and 111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment filed September 29, 2008 has been received and entered. Claims 1-102, and 109 have been cancelled, and new claim 111 has been added. Consequently claims 103-108 and 110-111 are pending in the instant application, of which claims 105-106 and sequences other than the elected SEQ ID NO: 2 have been withdrawn from further consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

1. The rejection of claims 103-104, and 107-108 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting programmed cell death in ***plant*** eukaryotes with SEQ ID NO: 2, does not reasonably provide enablement for inhibiting programmed cell death in ***all eukaryotes with any bacterial effector protein***. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Additionally, this rejection is applied to newly added claim 111.

Applicants assert that Example 7 of the present specification shows that programmed cell death can be suppressed in yeast by use of AvrPtoB. Applicants conclude that in view of the ability of the bacterial effector proteins of the present application to suppress programmed cell death in plants and yeast, one of ordinary skill in the art would expect such bacterial effector proteins to suppress cell death in any

eukaryote.

Applicants arguments have been fully considered but are not found to be persuasive.

First, Applicants assert that Example 7 of the present specification shows that programmed cell death can be suppressed in yeast by use of AvrPtoB. However, Applicants are respectfully directed back to their own claim language. Claim 103 recites methods of inhibiting programmed cell death in ***a eukaryote*** comprising administering ***a bacterial effector protein***." (Emphasis added). Simply stated the claims are neither limited to a eukaryote which is yeast, nor are they limited to the described molecule of AvrPtoB. Applicants single species of AvrPtoB inhibiting programmed cell death in yeast is not commensurate in scope with any bacterial effector protein inhibiting programmed cell death in any eukaryote.

Second, Applicants Example 7 demonstrates the unpredictability of bacterial effector proteins to inhibit programmed cell death in different eukaryotes when challenged with different molecules. Example 7 sets forth that AvrPtoB protected yeast from programmed cell death when challenged with H_2O_2, menadione and heat shock. "However, AvrPtoB, did not suppress Bax-induced cell death in yeast, suggesting differences exist between Bax and AvrPtoB functions in N. benthamiana and yeast." (See Specification page 49).

To further address these differences the following new reference is applied: US Patent 5,837,838.

Reed (US Patent 5,837,838) set forth that "the action of a Bax inhibitor protein is,

in fact, cell type specific and, in some cases, expression of a Bax inhibitor protein in a cell can increase the likelihood that the cell will undergo apoptosis." (See detailed paragraph number 4). Reed et al further disclose that "cell death that occurs in Bax-expressing yeast resembles that in mammalian cells ***when treated with Caspase inhibitors***." (Emphasis added, see detailed paragraph number 47). This is due to there being no evidence of Caspase-like proteolytic activities in yeast. (Detailed paragraph number 47 again).

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

First, Laccomme et al (PNAS Vol. 96, pp 7956-7961, 1999) set forth that programmed cell death (PCD) fulfills the same roles, elimination of unwanted cells during development and sacrifice of diseased cells, in both plants and animals.

However, "although some similarities exist between the ultrastructural and physiological hallmarks of PCD in animals and plants, evidence for common pathways leading to cell death is ***limited***." (Emphasis added, see page 7956). This teaching directly addresses factors 1-2, 4-5, and 7-8.

Reed (US Patent 5,837,838) set forth that "the action of a Bax inhibitor protein is, in fact, cell type specific and, in some cases, expression of a Bax inhibitor protein in a cell can increase the likelihood that the cell will undergo apoptosis." (See detailed paragraph number 4). Reed et al further disclose that "cell death that occurs in Bax-expressing yeast resembles that in mammalian cells ***when treated with Caspase inhibitors***." (Emphasis added, see detailed paragraph number 47). This is due to there being no evidence of Caspase-like proteolytic activities in yeast. (Detailed paragraph number 47 again). This teaching directly addresses factors 1-2, 4-5 and 7-8 and greatly questions the applicability of results obtained in yeast as being maintained in higher eukaryotes.

Finally, Applicants specification provides no guidance as to how to overcome this lack of common pathways between eukaryotic plant cells and eukaryotic mammalian cells, i.e., no working examples of eukaryotic cells other than plant cells or yeast, which as shown above cannot be extrapolated to higher eukaryotes. This directly addresses factor 3.

Given the lack of guidance, lack of working examples, and the unpredictable nature of the invention, one of skill in the art would be forced into excessive experimentation in order to practice the instantly claimed invention.

For reasons of record, as well as the reasons set forth above, this rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. The rejection of claims 103, 107 and 110 under 35 U.S.C. 102(b) as being anticipated by Nimchuk et al is maintained.

Applicants amendment to claims 104 and 108 are sufficient to overcome this rejection.

Applicants assert that Nimchuk does not characterize the administration of bacterial effector proteins to eukaryote plant cells as inhibiting cell death. Applicants further assert that Nimchuk does just the opposite, i.e., it induces cell death, also known as a hypersensitive response.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants assert that Nimchuk does not characterize the administration of bacterial effector proteins to eukaryote plant cells as inhibiting cell death. However, Applicants are respectfully directed to the teachings of Nimchuk et al. Nimchuk et al disclose of the identical method steps as claimed, administering to a eukaryotic cell a bacterial effector protein. (See pages 353-354). Any result of "inhibiting programmed cell death" would be a direct and inherent consequence of administering the identical molecule as claimed to the identical cell as claimed.

Finally, Applicants assert that Nimchuk does just the opposite, i.e., it induces cell death, also known as a hypersensitive response. However, Applicants assertions appear to be a stement of conclusion. Applicants do not point to any particular part of the reference which discloses this result. The question remains, how is it possible to administer a bacterial effector protein to a eukaryote and inhibit programmed cell death as instantly claimed, while the prior art did the exact same thing, (administer a bacterial effector protein to a eukaryote) but not inhibit programmed cell death? If the protein was different (e.g., SEQ ID NO: 2) this could readily be explained, however the claim would need to reflect this difference over the teachings of the prior art.

The claims are directed to a method of inhibiting programmed cell death in a eukaroyote, said method comprising administering to the eukaryote a bacterial effector protein which inhibits programmed cell death.

Nimchuk et al (Cell Vol. 101, pp 353-363, May 2000) disclose of delivering

bacterial effector proteins to eukaryotic plant cells. (See pages 353-354).

It is noted that Nimchuk et al do not characterize the administration of bacterial effector proteins to eukaryotic plant cells as inhibiting programmed cell death, however, given that Nimchuk et al combined eukaryotic plant cells as claimed, with the structurally identical bacterial effector proteins, also as claimed, any property of inhibiting programmed cell death is a necessarily inherent result from combining eukaryotic cells and bacterial effector proteins as claimed.

Furthermore, claim 107 has been included in this rejection for reciting "comprises the amino acid sequence spanning a C-terminus of SEQ ID NO: 2." This allows for short subsequences of the C-terminus (e.g., single carboxy amino acid only) of SEQ ID NO: 2, and given that the bacterial effector protein delivered to eukaryotic plant cells by Nimchuk et al shares short "C-terminus subsequences" in common with SEQ ID NO: 2, the disclosure of Nimchuk et al is deemed to anticipate the claimed invention.

For reasons of record, as well as the reasons set forth above, this rejection is maintained for reasons of record.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Navarro/
Primary Examiner, Art Unit 1645
January 2, 2009